Remarks

Applicants submit their election to previously issued restriction requirement and also request amendments to the claims be entered prior to search and examination.

Applicants' Election

The examiner has restricted applicants' claims as defining four separate inventions as defined by the following groupings:

I. Claims 1-34 and 44-76, drawn to a treatment system comprising a catheter, classified in class 435, subclass 226.
II. Claims 35-43, drawn to a method for identifying a therapeutic protein and associating the protein with a transport aid, classified in class 435, subclass 15.
III. Claims 77-128, drawn to a method of treatment using catheter and a therapeutic protein, classified in class 424, subclass 94.1.

Applicants, elected Group I, claims 1-34 and 44-76, which is drawn to a treatment system comprising a catheter, classified in class 435, subclass 226. Applicants have cancelled the remaining claims 35-43 and 77-128, without prejudice. Applicants reserve the right to file one or more future divisional applications, should Applicants' request to remove the present restriction requirement not be granted.

Having elected Invention I, applicants were required to elect one or more of the following sub-Inventions:

(A) A disease of Claims 2-4, 29-31, and 55-57.
Applicants elect the disease mucopolysaccharidosis of claim 3.

(B) A catheter without or; **(C)** A catheter with a protein.
Applicants elect (C) a catheter with a protein of claim.

Having elected (C) a catheter with a protein, Applicants were required to further elect one of the proteins in Claims 6-7 and 59-60.
Applicants elect alpha-L-iduronidase of claim 6.

Having elected (C) a catheter with a protein, Applicants were required to further elect (D) with protein modification or (E) without protein modification.

Applicants elect (D) a protein with modification

Having elected Invention I, Applicants were to elect on of the locations of Claim 45 and 69.

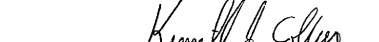
Applicants elect the intracerebroventricular location of claims 45 and 69.

Applicants also indicate that withdrawal of claims to the non-elected invention has not changed the inventorship Originally set forth, and therefore is in compliance with 37 CFR 1.48(b).

Applicants Preliminary Amendments to the Claims

Applicants respectfully request that amendments to claims 1, 28, and 54 be entered prior to search and examination of the present invention I.

Respectfully submitted,



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PENDING CLAIMS AS AMENDED
(MARKED UP VERSION)

1. (Amended) A system comprising:

a) a therapeutic protein formulation that has been modified for enhanced cellular uptake properties; and

b) an implantable catheter system to physically deliver said therapeutic protein formulation across the blood-brain barrier of patients for the purpose of treating said patients having neurological diseases of the central nervous system[.], and

(c) a pump that pumps said therapeutic protein formulation through said implantable catheter system to at least one targeted region,

wherein the pump provides for a programmable delivery rate of the therapeutic protein formulation, and wherein the delivery rate is selected based on factors selected from the group consisting of specific neurological disease, genetic sequence of the patient's gene encoding for the protein to be delivered, body weight, and combinations thereof.

2. (Original) The system of claim 1, wherein the neurological diseases treated are selected from the group consisting of lysosomal storage diseases, protein deficiency diseases, enzyme deficiency diseases, inborn errors of metabolism, neurodegenerative diseases, and combinations thereof.

3. (Original) The system of claim 1, wherein said neurological diseases are inborn errors of metabolism selected from the group consisting of gangliosidosis, sphingolipidosis, glycoprotein disorders, glycogen storage diseases, mucolipidosis, mucopolysaccharidosis, · cholesterol ester storage disease, farber lipogranulomatosis, galactosialidosis type I, galactosialidosis type II, neuronal ceroid lipofuscinosis, and combinations thereof.

4. (Original) The system of claim 1, wherein said neurological diseases are selected from the group consisting of Fragile X Syndrome, Parkinson's disease, Alzheimer's disease, and combinations thereof.

5. (Original) The system of claim 1, wherein the therapeutic protein formulation comprises enzymes providing for enzyme replacement therapy.

6. (Original) The system of claim 5, wherein the enzymes are selected from the group consisting of beta-glucosidase, glucocerebrosidase, acid sphingomyelinase, galactocerebrosidase, arylsulfatase A, saposin B, alpha-galactosidase A, beta-galactosidase, beta-hexosaminidase A, beta-hexosaminidase A and B, alpha-L-fucosidase, alpha-D-mannosidase, beta-D-mannosidase, N-aspartyl-beta-glucosaminidase, alpha-glucosidase, LAMP-2, glycogen branching enzyme, neuraminidase, phosphotransferase, alpha-L-iduronidase, iduronate-2-sulfatase, heparan-N-sulfatase, alpha-N-acetylglucosaminidase, acetylCoA:N-acetyltransferase, N-acetylglucosamine 6-sulfatase, galactose 6-sulfatase, beta-galactosidase, N-acetylgalactosamine 4-sulfatase, beta-glucuronidase, lysosomal acid lipase, acid cholesteryl ester hydrolase, acid ceramidase, N-acetyl-alpha-D-galactosaminidase, palmitoyl protein thioesterase, and combinations thereof.

7. (Original) The system of claim 1, wherein the therapeutic protein formulation comprises proteins selected from the group consisting of GDNF, FMRP, and combinations thereof.

8. (Original) The system of claim 1, wherein at least some of the proteins within said therapeutic protein formulation have been modified to comprise a transport aid that provides for enhanced cellular uptake of said modified proteins.

9. (Original) The system of claim 8, wherein said modified proteins have been modified by incorporating into their structure amino acid sequences providing for an intrinsic transport aid.

10. (Original) The system of claim 9, wherein said modified proteins are fusion proteins.

11. (Original) The system of claim 8, wherein said modified proteins have been modified by conjugation to a transport aid that facilitates the cellular uptake of said therapeutic protein.

12. (Original) The system of claim 11, wherein the transport aid comprises at least a portion of a species selected from the group consisting of recombinant human melanotransferrin, p97, tetanus toxin fragment C, endogenous lectins, biotin, and combinations thereof.

13. (Original) The system of claim 11, wherein the conjugation comprises a linker species existing between said therapeutic protein and said transport aid.

14. (Original) The system of claim 13, wherein said linker is selected from the group consisting of peptide linkages, disulfide linkages, and combinations thereof.

15. (Original) The system of claim 13, wherein said linker is a streptavidin-biotin complex.

16. (Original) The system of claim 1, wherein said therapeutic protein formulation has been formulated to help maintain the integrity and activity of the protein formulation.

17. (Original) The system of claim 16, wherein the integrity and activity of the protein formulation is achieved by the addition to said therapeutic protein formulation, at least one species operable for maintaining a desired pH.

18. (Original) The system of claim 1, wherein said implantable catheter system is implanted so as to deliver said therapeutic protein formulation to regions selected from the group consisting of intrathecal, intraparenchymal, intracerebroventricular, and combinations thereof.

19. (Original) The system of claim 1, further comprising an inlet for the introduction of therapeutic protein formulation to the implanted catheter system.

20. (Original) The system of claim 1, further comprising a reservoir to contain said therapeutic protein formulation prior to delivery.

21. (Original) The system of claim 20, wherein said reservoir is implantable and refillable.

22. (Cancel) The system of claim 1, further comprising a pump that pumps said therapeutic protein formulation through said implantable catheter system to at least one targeted region.

23. (Original) The system of claim 22, wherein the pump comprises an integrated reservoir.

24. (Original) The system of claim 22, wherein said pump is implantable.

25. (Original) The system of claim 1, wherein the implantable catheter system comprises at least one branched catheter permitting delivery to at least two separate regions using one primary catheter line.

26. (Original) The system of claim 25, wherein the branched catheter is bifurcated.

27. (Cancel) The system of claim 22, wherein the pump provides for a programmable delivery rate of the therapeutic protein formulation, and wherein the delivery rate is selected based on factors selected from the group consisting of specific neurological disease, genetic sequence of the patient's gene encoding for the protein to be delivered, body weight, and combinations thereof.

28. (Amended) A system comprising:
a) a means of providing for a therapeutic protein formulation that facilitates cellular uptake of proteins within said formulation; and
b) a means of physically bypassing the blood-brain barrier, via an implantable catheter system, so as to deliver said therapeutic protein formulation to target cells

for the purpose of treating neurological diseases of the central nervous system[.] and

(c) a pump that pumps said therapeutic protein formulation through said implantable catheter system to at least one targeted region,

wherein the pump provides for a programmable delivery rate of the therapeutic protein formulation, and wherein the delivery rate is selected based on factors selected from the group consisting of specific neurological disease, genetic sequence of the patient's gene encoding for the protein to be delivered, body weight, and combinations thereof.

29. (Original) The system of claim 28, wherein the neurological diseases to be treated are selected from the group consisting of lysosomal storage diseases, protein deficiency diseases, enzyme deficiency diseases, inborn errors of metabolism, neurodegenerative diseases, and combinations thereof.

30. (Original) The system of claim 28, wherein said neurological diseases are inborn errors of metabolism selected from the group consisting of gangliosidosis, sphingolipidosis, glycoprotein disorders, glycogen storage diseases, mucolipidosis, mucopolysaccharidosis, cholesterol ester storage disease, farber lipogranulomatosis, galactosialidosis type I, galactosialidosis type II, neuronal ceroid lipofuscinosis, and combinations thereof.

31. (Original) The system of claim 28, wherein said neurological diseases are selected from the group consisting of Fragile X Syndrome, Parkinson's disease, Alzheimer's disease, and combinations thereof.

32. (Original) The system of claim 28, wherein the therapeutic protein formulation comprises enzymes providing for enzyme replacement therapy.

33. (Original) The system of claim 32, wherein the enzymes are selected from the group consisting of beta-glucosidase, glucocerebrosidase, acid sphingomyelinase, galactocerebrosidase, arylsulfatase A, saposin B, alpha-galactosidase A, beta-galactosidase, beta-hexosaminidase A, beta-hexosaminidase A and B, alpha-L-

fucosidase, alpha-D-mannosidase, beta-D-mannosidase, N-aspartyl-beta-glucosaminidase, alpha-glucosidase, LAMP-2, glycogen branching enzyme, neuraminidase, phosphotransferase, alpha-L-iduronidase, iduronate-2-sulfatase, heparan-N-sulfatase, alpha-N-acetylglucosaminidase, acetylCoA:N-acetyltransferase, N-acetylglucosamine 6-sulfatase, galactose 6-sulfatase, beta-galactosidase, N-acetylgalactosamine 4-sulfatase, beta-glucuronidase, lysosomal acid lipase, acid cholesteryl ester hydrolase, acid ceramidase, N-acetyl-alpha-D-galactosaminidase, palmitoyl protein thioesterase, and combinations thereof.

34. (Original) The system of claim 28, wherein the therapeutic protein formulation comprises proteins selected from the group consisting of GDNF, FMRP, and combinations thereof.

35. (Cancel) The system of claim 28, wherein the means of providing for a protein formulation that facilitates cellular uptake of proteins within said formulation, for the purpose of treating neurological diseases of the central nervous system, further comprises:

a) a means of identifying and selecting at least one appropriate therapeutic protein material, appropriate for use in treating a particular neurological disease of the central nervous system; and

b) a means of associating at least one transport aid with the said at least one appropriate therapeutic protein material for the purpose of facilitating cellular uptake of the therapeutic protein material.

36. (Cancel) The system of claim 35, wherein the means of identifying and selecting at least one appropriate therapeutic protein material, appropriate for use in treating a particular neurological disease of the central nervous system comprises a medical diagnostic protocol.

37. (Cancel) The system of claim 35, wherein the means of associating at least one transport aid with the said at least one appropriate therapeutic protein material for the purpose of facilitating cellular uptake involves a modification by incorporation of at least one amino acid sequence into the said at least one appropriate therapeutic

protein material structure so as to provide for therapeutic protein material comprising intrinsic transport aids.

38. (Cancel) The system of claim 37, wherein said therapeutic protein material comprising an intrinsic transport aid is comprised of fusion proteins.

39. (Cancel) The system of claim 35, wherein the means of associating at least one transport aid with the said at least one appropriate therapeutic protein material for the purpose of facilitating cellular uptake involves a modification of at least some of the therapeutic proteins within said therapeutic protein formulation, wherein said modified therapeutic proteins are modified by conjugating to them a transport aid that facilitates the cellular uptake of said modified therapeutic proteins.

40. (Cancel) The system of claim 39, wherein the transport aid comprises at least a portion of a species selected from the group consisting of recombinant human melanotransferrin, p97, tetanus toxin fragment C, endogenous lectins, biotin, and combinations thereof.

41. (Cancel) The system of claim 39, wherein the modification by conjugating comprises a linker species existing between said therapeutic protein and said transport aid.

42. (Cancel) The system of claim 41, wherein said linker is selected from the group consisting of peptide linkages, disulfide linkages, and combinations thereof.

43. (Cancel) The system of claim 41, wherein said linker is a streptavidin-biotin complex.

44. (Original) The system of claim 28, wherein said therapeutic protein formulation is formulated to help maintain the integrity and activity of the protein formulation.

45. (Original) The system of claim 28, wherein the means of physically bypassing the blood-brain barrier so as to deliver said therapeutic protein formulation to target

cells comprising positioning said implanted catheter system so as to deliver said therapeutic protein formulation in a manner selected from the group consisting of intrathecally, intraparenchymally, intracerebroventricularly, and combinations thereof.

46. (Original) The system of claim 28, wherein said implanted catheter system comprises a branched catheter.

47. (Original) The system of claim 46, wherein the branched catheter is a bifurcated catheter to allow for the delivery of protein formulation to two regions with a single catheter.

48. (Original) The system of claim 28, further comprising a reservoir to contain said protein formulation prior to delivery.

49. (Original) The system of claim 48, wherein said reservoir is implantable and refillable.

50. (Cancel) The system of claim 28, further comprising a pump that pumps said protein formulation through said implantable catheter system to at least one targeted region.

51. (Original) The system of claim 50, wherein the pump comprises an integrated reservoir.

52. (Original) The system of claim 50, wherein said pump is implantable.

53. (Cancel) The system of claim 50, wherein the pump provides for a programmable delivery rate of the therapeutic protein formulation, and wherein the delivery rate is selected based on factors selected from the group consisting of specific neurological disease, genetic sequence of the patient's gene encoding for the protein to be delivered, body weight, and combinations thereof.

54. (Amended) A system comprising:

a) a therapeutic protein formulation; and

b) an implantable catheter system comprising a programmable pump to physically deliver said therapeutic protein formulation across the blood-brain barrier at a programmed delivery rate for the purpose of treating patients diagnosed with at least one neurological disease of the central nervous system[.]

(c) a pump that pumps said therapeutic protein formulation through said implantable catheter system to at least one targeted region,

wherein the pump provides for a programmable delivery rate of the therapeutic protein formulation, and wherein the delivery rate is selected based on factors selected from the group consisting of specific neurological disease, genetic sequence of the patient's gene encoding for the protein to be delivered, body weight, and combinations thereof.

55. (Original) The system of claim 54, wherein the neurological disease treated are selected from the group consisting of lysosomal storage diseases, protein deficiency diseases, enzyme deficiency diseases, inborn errors of metabolism, neurodegenerative diseases, and combinations thereof.

56. (Original) The system of claim 54, wherein said at least one neurological disease is an inborn error of metabolism selected from the group consisting of gangliosidosis, sphingolipidosis, glycoprotein disorders, glycogen storage diseases, mucolipidosis, mucopolysaccharidosis, cholesterol ester storage disease, farber lipogranulomatosis, galactosialidosis type I, galactosialidosis type II, neuronal ceroid lipofuscinosis, and combinations thereof.

57. (Original) The system of claim 54, wherein said at least one neurological disease is selected from the group consisting of Fragile X Syndrome, Parkinson's disease, Alzheimer's disease, and combinations thereof.

58. (Original) The system of claim 54, wherein the therapeutic protein formulation comprises enzymes providing for enzyme replacement therapy.

59. (Original) The system of claim 58, wherein the enzymes are selected from the group consisting of beta-glucosidase, glucocerebrosidase, acid sphingomyelinase, galactocerebrosidase, arylsulfatase A, saposin B, alpha-galactosidase A, beta-galactosidase, beta-hexosaminidase A, beta-hexosaminidase A and B, alpha-L-fucosidase, alpha-D-mannosidase, beta-D-mannosidase, N-aspartyl-beta-glucosaminidase, alpha-glucosidase, LAMP-2, glycogen branching enzyme, neuraminidase, phosphotransferase, alpha-L-iduronidase, iduronate-2-sulfatase, heparan-N-sulfatase, alpha-N-acetylglucosaminidase, acetylCoA:N-acetyltransferase, N-acetylglucosamine 6-sulfatase, galactose 6-sulfatase, beta-galactosidase, N-acetylgalactosamine 4-sulfatase, beta-glucuronidase, lysosomal acid lipase, acid cholesteryl ester hydrolase, acid ceramidase, N-acetyl-alpha-D-galactosaminidase, palmitoyl protein thioesterase, and combinations thereof.

60. (Original) The system of claim 54, wherein the therapeutic protein formulation comprises proteins selected from the group consisting of GDNF, FMRP, and combinations thereof.

61. (Original) The system of claim 54, wherein at least some of the proteins within said therapeutic protein formulation have been modified to comprise a transport aid that provides for enhanced cellular uptake of said modified proteins.

62. (Original) The system of claim 61, wherein said modified proteins have been modified by incorporating into their structure amino acid sequences providing for an intrinsic transport aid.

63. (Original) The system of claim 62, wherein said modified proteins are fusion proteins.

64. (Original) The system of claim 61, wherein said modified proteins have been modified by conjugation to a transport aid that facilitates the cellular uptake of said therapeutic protein.

65. (Original) The system of claim 64, wherein the transport aid comprises at least a portion of a species selected from the group consisting of recombinant human melanotransferrin, p97, tetanus toxin fragment C, endogenous lectins, biotin, and combinations thereof.

66. (Original) The system of claim 64, wherein the conjugation comprises a linker species existing between said therapeutic protein and said transport aid.

67. (Original) The system of claim 66, wherein said linker is a streptavidin-biotin complex.

68. (Original) The system of claim 54, wherein said therapeutic protein formulation has been formulated to help maintain the integrity and activity of the protein formulation.

69. (Original) The system of claim 54, wherein said implantable catheter system is implanted so as to deliver said therapeutic protein formulation to regions selected from the group consisting of intrathecal, intraparenchymal, intracerebroventricular, and combinations thereof.

70. (Original) The system of claim 54, further comprising an inlet for the introduction of therapeutic protein formulation to the implanted catheter system.

71. (Original) The system of claim 54, further comprising a reservoir to contain said therapeutic protein formulation prior to delivery.

72. (Original) The system of claim 71, wherein said reservoir is implantable and refillable through a subcutaneous inlet.

73. (Original) The system of claim 54, wherein the programmable pump comprises an integrated reservoir.

74. (Original) The system of claim 54, wherein said programmable pump is implantable.

75. (Original) The system of claim 54, wherein the implantable catheter system comprises at least one branched catheter permitting delivery to at least two separate regions using one primary catheter line.

76. (Cancel) The system of claims 54, wherein the programmable pump provides for a variable delivery rate of the therapeutic protein formulation, and wherein the delivery rate is selected based on factors selected from the group consisting of specific neurological disease, genetic sequence of the patient's gene encoding for the protein to be delivered, body weight, and combinations thereof.

77. (Cancel) A method comprising the steps of:

a) providing a therapeutic protein formulation comprising proteins that have been modified for enhanced cellular uptake; and

b) physically delivering said therapeutic protein formulation across the blood brain barrier of patients, via an implantable catheter system, for the purpose of treating neurological diseases of the central nervous system.

78. (Cancel) The method of claim 77, wherein the therapeutic protein formulation is delivered in a manner selected from the group consisting of intrathecally, intraparenchymally, intracerebroventricularly, and combinations thereof.

79. (Cancel) The method of claim 77, wherein the neurological diseases to be treated are selected from the group consisting of lysosomal storage diseases, protein deficiency diseases, enzyme deficiency diseases, inborn errors of metabolism, neurodegenerative diseases, and combinations thereof.

80. (Cancel) The method of claim 77, wherein said neurological diseases are inborn errors of metabolism selected from the group consisting of gangliosidosis, sphingolipidosis, glycoprotein disorders, glycogen storage diseases, mucolipidosis, mucopolysaccharidosis, cholesterol ester storage disease, farber

lipogranulomatosis, galactosialidosis type I, galactosialidosis type II, neuronal ceroid lipofuscinosis, and combinations thereof.

81. (Cancel) The method of claim 77, wherein said neurological diseases are selected from the group consisting of Fragile X Syndrome, Parkinson's disease, Alzheimer's disease, and combinations thereof.

82. (Cancel) The method of claim 77, wherein the therapeutic protein formulation comprises enzymes providing for enzyme replacement therapy.

83. (Cancel) The method of claim 82, wherein the enzymes are selected from the group consisting of beta-glucosidase, glucocerebrosidase, acid sphingomyelinase, galactocerebrosidase, arylsulfatase A, saposin B, alpha-galactosidase A, beta-galactosidase, beta-hexosaminidase A, beta-hexosaminidase A and B, alpha-L-fucosidase, alpha-D-mannosidase, beta-D-mannosidase, N-aspartyl-beta-glucosaminidase, alpha-glucosidase, LAMP-2, glycogen branching enzyme, neuraminidase, phosphotransferase, alpha-L-iduronidase, iduronate-2-sulfatase, heparan-N-sulfatase, alpha-N-acetylglucosaminidase, acetylCoA:N-acetyltransferase, N-acetylglucosamine 6-sulfatase, galactose 6-sulfatase, beta-galactosidase, N-acetylgalactosamine 4-sulfatase, beta-glucuronidase, lysosomal acid lipase, acid cholesteryl ester hydrolase, acid ceramidase, N-acetyl-alpha-D-galactosaminidase, palmitoyl protein thioesterase, and combinations thereof.

84. (Cancel) The method of claim 77, wherein the therapeutic protein formulation comprises proteins selected from the group consisting of GDNF, FMRP, and combinations thereof.

85. (Cancel) The method of claim 77, wherein at least some of the proteins within said therapeutic protein formulation are modified so as to comprise a transport aid that provides for enhanced cellular uptake of said modified proteins.

86. (Cancel) The method of claim 85, wherein said modified proteins are modified by incorporating into their structure amino acid sequences providing for an intrinsic transport aid.

87. (Cancel) The method of claim 86, wherein said modified proteins are fusion proteins.

88. (Cancel) The method of claim 85, wherein said modified proteins are modified by conjugating to them a transport aid that facilitates the cellular uptake of said therapeutic protein.

89. (Cancel) The method of claim 88, wherein the transport aid comprises at least a portion of a species selected from the group consisting of recombinant human melanotransferrin, p97, tetanus toxin fragment C, endogenous lectins, biotin, and combinations thereof.

90. (Cancel) The method of claim 88, wherein the modification by conjugating comprises at least one linker species existing between said therapeutic protein and said transport aid.

91. (Cancel) The method of claim 90, wherein said linker is selected from the group consisting of peptide linkages, disulfide linkages, and combinations thereof.

92. (Cancel) The method of claim 88, wherein the conjugation is non-covalent.

93. (Cancel) The method of claim 90, wherein said linker is a streptavidin-biotin complex.

94. (Cancel) The method of claim 77, wherein said therapeutic protein formulation is formulated to help maintain the integrity and activity of the protein formulation.

95. (Cancel) The method of claim 77, wherein said therapeutic protein formulation is introduced into the said implantable catheter system via an injection port.

96. (Cancel The method of claim 77, wherein said therapeutic protein formulation is held in a reservoir.

97. (Cancel) The method of claim 96, wherein the reservoir is implantable and refillable.

98. (Cancel) The method of claim 77, further comprising a pump to direct therapeutic protein formulation through said implantable catheter and into a target region.

99. (Cancel) The method of claim 98, wherein the pump comprises a integrated reservoir.

100. (Cancel) The method of claim 98, wherein the pump is implantable.

101. (Cancel) The method of claim 77, wherein said implantable catheter system comprises at least one bifurcated catheter.

102. (Cancel) The method of claim 98, wherein the pump provides for a programmable delivery rate of the therapeutic protein formulation, and wherein the delivery rate is selected based on factors selected from the group consisting of specific neurological disease, genetic sequence of the patient's gene encoding for the protein to be delivered, body weight, and combinations thereof.

103. (Cancel) A therapy comprising:
a) a therapeutic protein formulation comprising proteins that have been modified for enhanced cellular uptake; and
b) the physical delivery of said therapeutic protein formulation across the blood brain barrier of patients, via an implantable catheter system, for the purpose of treating neurological diseases of the central nervous system.

104. (Cancel) The therapy of claim 103, wherein the therapeutic protein formulation is delivered in a manner selected from the group consisting of intrathecally, intraparenchymally, intracerebroventricularly, and combinations thereof.

105. (Cancel) The therapy of claim 103, wherein the neurological diseases to be treated are selected from the group consisting of lysosomal storage diseases, protein deficiency diseases, enzyme deficiency diseases, inborn errors of metabolism, neurodegenerative diseases, and combinations thereof.

106. (Cancel) The therapy of claim 103, wherein said neurological diseases are inborn errors of metabolism selected from the group consisting of gangliosidosis, sphingolipidosis, glycoprotein disorders, glycogen storage diseases, mucolipidosis, mucopolysaccharidosis, cholesterol ester storage disease, farber lipogranulomatosis, galactosialidosis type I, galactosialidosis type II, neuronal ceroid lipofuscinosis, and combinations
thereof.

107. (Cancel) The therapy of claim 103, wherein said neurological diseases are selected from the group consisting of Fragile X Syndrome, Parkinson's disease, Alzheimer's disease, and combinations thereof.

108. (Cancel) The therapy of claim 103, wherein the therapeutic protein formulation comprises enzymes providing for enzyme replacement therapy.

109. (Cancel) The therapy of claim 108, wherein the enzymes are selected from the group consisting of beta-glucosidase, glucocerebrosidase, acid sphingomyelinase, galactocerebrosidase, arylsulfatase A, saposin B, alpha-galactosidase A, beta-galactosidase, beta-hexosaminidase A, beta-hexosaminidase A and B, alpha-L-fucosidase, alpha-D-mannosidase, beta-D-mannosidase, N-aspartyl-beta-glucosamiminidase, alpha-glucosidase, LAMP-2, glycogen branching enzyme, neuraminidase, phosphotransferase, alpha-L-iduronidase, iduronate-2-sulfatase, heparan-N-sulfatase, alpha-N-acetylglucosaminidase, acetylCoANacetyltransferase, N-acetylglucosamine 6-sulfatase, galactose 6-sulfatase, beta-galactosidase, N-acetylgalactosamine 4-sulfatase, beta-glucuronidase, lysosomal acid lipase, acid cholesteryl ester hydrolase, acid ceramidase, N-acetyl-alpha-D-galactosaminidase, palmitoyl protein thioesterase, and combinations thereof.

110. (Cancel) The therapy of claim 103, wherein the therapeutic protein formulation comprises proteins selected from the group consisting of GDNF, FMRP, and combinations thereof.

111. (Cancel) The therapy of claim 103, wherein at least some of the proteins within said therapeutic protein formulation are modified so as to comprise a transport aid that provides for enhanced cellular uptake of said modified proteins.

112. (Cancel) The therapy of claim 111, wherein said modified proteins are modified by incorporating into their structure amino acid sequences providing for an intrinsic transport aid.

113. (Cancel) The therapy of claim 112, wherein said modified proteins are fusion proteins.

114. (Cancel) The therapy of claim 111, wherein said modified proteins are modified by conjugating to them a transport aid that facilitates the cellular uptake of said therapeutic protein.

115. (Cancel) The therapy of claim 114, wherein the transport aid comprises at least a portion of a species selected from the group consisting of recombinant human melanotransferrin, p97, tetanus toxin fragment C, endogenous lectins, biotin, and combinations thereof.

116. (Cancel) The therapy of claim 114, wherein the modification by conjugating comprises at least one linker species existing between said therapeutic protein and said transport aid.

117. (Cancel) The therapy of claim 116, wherein said linker is selected from the group consisting of peptide linkages, disulfide linkages, and combinations thereof.

118. (Cancel) The therapy of claim 114, wherein the conjugation is non-covalent.

119. (Cancel) The therapy of claim 116, wherein said linker is a streptavidin-biotin complex.

120. (Cancel) The therapy of claim 103, wherein said therapeutic protein formulation is formulated to help maintain the integrity and activity of the protein formulation.

121. (Cancel) The therapy of claim 103, wherein said therapeutic protein formulation is introduced into the said implantable catheter system via an injection port.

122. (Cancel) The therapy of claim 103, wherein said therapeutic protein formulation is held in a reservoir.

123. (Cancel) The therapy of claim 122, wherein the reservoir is implantable and refillable via a subcutaneous inlet.

124. (Cancel) The therapy of claim 103, further comprising a pump to direct therapeutic protein formulation through said implantable catheter and into a target region.

125. (Cancel) The therapy of claim 124, wherein the pump comprises a integrated reservoir.

126. (Cancel) The therapy of claim 124, wherein the pump is implantable.

127. (Cancel) The therapy of claim 103, wherein said implantable catheter system comprises at least one bifurcated catheter.

128. (Cancel) The therapy of claim 124, wherein the pump provides for a programmable delivery rate of the therapeutic protein formulation, and wherein the delivery rate is selected based on factors selected from the group consisting of

specific neurological disease, genetic sequence of the patient's gene encoding for the protein to be delivered, body weight, and combinations thereof.